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SOLVENT EFFECTS ON ENDO/EXO SELECTIVITIES IN (4 + 2) CYCLOADDITIONS OF CYANOETHYLENES.

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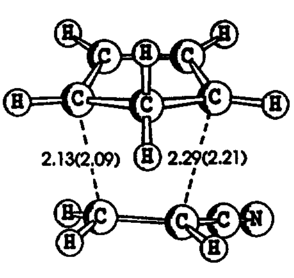
Abstract: SCRF calculations on transition structures of cycloadditions of acrylonitrile and maleonitrile to cyclopentadiene and 1,3-butadiene show that the experimentally observed endo preference for the cycloaddition of acrylonitrile to cyclopentadiene is the consequence of solvent influence and not the result of secondary orbital interactions.

Secondary orbital overlap has been suggested by Woodward and Hoffmann[1] as the main reason to explain the preference for endo addition in many (4 + 2) cycloadditions.[2] Although appealing and easy to understand by simple frontier molecular orbital (FMO) arguments, questions as to the soundness of this approach remain. At the time when the proposal was made no detailed knowledge about transition structures for (4 + 2) cycloadditions existed. Therefore, it was also not possible to know the separation of the atoms involved in secondary orbital overlap in the transition structures (TS). This knowledge alone will already allow an estimate of the importance of the effect.

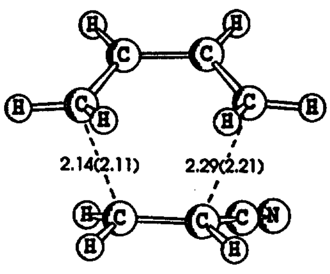
A number of ab-initio and semiempirical calculations on transition structures for (4 + 2) cycloadditions have been carried out.[3,4] Interestingly, when endo/exo selectivity was involved they have not provided agreement between theory and experiment. The best ab-initio calculation for the cycloaddition of cyclopentadiene to acrylonitrile so far have led to a 0.2 kcal mol^{-1} preference for exo addition,[5] although the experiment suggests just the opposite by about the same amount.[6,7] We like to suggest that it is the influence of the medium which causes the endo preference and that secondary orbital interactions are not involved.

Recently, it became possible to evaluate the influence of solvents on ground-state structures and reaction intermediates by applying the dielectric-continuum model of solvation in quantum-chemical calculations.[8,9] In this model the molecule is placed in a cavity surrounded by a dielectric continuum and the medium effect is taken into account iteratively (self consistent reaction field (SCRF)).

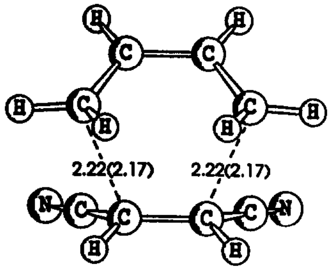
Cyanoalkenes have played a major role in determining the influence of substitutents on rates in Diels-Alder reactions.[6,7] The activation energies of their cycloadditions to cyclopentadiene are known. Semiempirical and ab-initio calculations have been carried out on these model reactions for normal Diels-Alder cycloadditions.[4,5] We used for our analysis the 3-21G ab-initio transition structures of Houk et al.[5] and determined also the MNDO PM3 TS for the cycloadditions of cyclopentadiene and 1,3-butadiene to acrylonitrile (1en,1ex,2en and 2ex) and for butadiene to maleonitrile (3en and 3ex). The semiempirically calculated geometries deviate only slightly from the ab-initio structures. In formulae 1 - 3 the ab-initio and semiempirical (in brackets) values of the separation in Å of the reacting atoms in the TS are indicated. As to the endo/exo selectivity ab-initio 3-21G and MNDO-PM3 lead to the same conclusion. Exo addition is preferred by ca. 0.2 - 0.6 kcal mol^{-1}. Table 1 reports data on the transition structures. The semiempirically determined activation energies are similar to the ab-initio values.



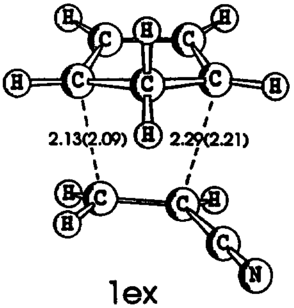
1en



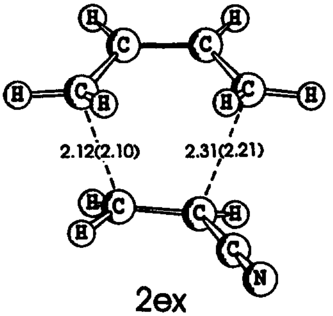
2en



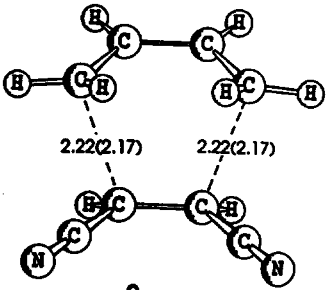
3en



1ex



2ex



3ex

SCRF calculations[9] were carried out by placing the transition structures in "dichloromethane" as solvent. A reoptimization of transition structures is not possible in the present version of the program GEOMOS. In order to see whether structural differences between ab-initio and semiempirical TS have an effect on the results we did the calculation for both TS (Table 1). As can be seen from the data the conclusions do not depend on the differences in structure. The intriguing result is that the solvent reverts the "gas-phase" preference for exo addition to an endo addition in all three cases, ranging from 0.05 kcal mol^{-1} for the 1,3-butadiene / acrylonitrile TS to 0.36, respectively 0.86 kcal mol^{-1} for the cyclopentadiene / acrylonitrile TS. The effect on the ab-initio structure is higher than on the "gas-phase" PM3 TS. Regardless of the absolute numbers the trend which the solvent exerts is important. The polarities of the TS seem to play a crucial role. In the "gas-phase" calculations the differences in dipole moment between the endo and exo TS of the cycloadditions of 1,3-butadiene to the cyanoalkenes are small, in the case of cyclopentadiene it is slightly higher. As soon as the TS are placed in solution the differences in dipole moment increase due to

Table 1: Energetics and dipole moments of transition structures of cycloadditions of cyanoalkenes to 1,3-dienes.

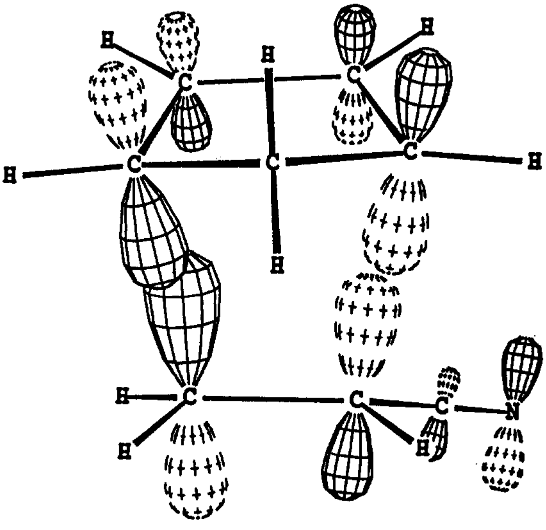
		RHF/3-21G	PM3 [b,c]	PM3 [b,c] in CH_2Cl_2	PM3-TS [b]	PM3-TS [b] in CH_2Cl_2
1en	energy	-360.4961027 [a]	117.337	112.53	114.88	110.15
	ZPVE [d]	99.82	-	-	-	-
	E_a [b]	26.0 [e]	-	-	32.95	32.08
	μ [D]	5.05	4.02	5.03	4.15	5.20
1ex	energy	-360.4965348 [a]	117.335	113.39	114.63	110.61
	ZPVE [d]	99.89	-	-	-	-
	E_a [b]	25.7 [e]	-	-	32.70	32.54
	μ [D]	4.69	3.46	4.34	3.60	4.56
2en	energy	-322.8261604 [a]	112.07	107.81	109.55	105.28
	ZPVE [d]	95.07	-	-	-	-
	E_a [b]	33.7 [e]	-	-	27.45	26.99
	μ [D]	4.50	3.54	4.39	3.68	4.56
2ex	energy	-322.8270524 [a]	111.80	118.05	109.11	105.33
	ZPVE [d]	95.11	-	-	-	-
	E_a [b]	33.1 [e]	-	-	27.01	26.99
	μ [D]	4.46	3.42	4.25	3.49	4.36
3en	energy	-414.0394984 [a]	150.97	144.38	147.71	140.57
	ZPVE [d]	94.60	-	-	-	-
	E_a [b]	32.2 [e]	-	-	28.67	30.48
	μ [D]	6.74	5.26	6.29	5.50	6.65
3ex	energy	-414.0401888 [a]	150.78	144.64	147.35	141.16
	ZPVE [d]	94.69	-	-	-	-
	E_a [b]	31.8 [e]	-	-	28.31	31.07
	μ [D]	6.85	5.25	6.42	5.47	6.73

a) in hartree; b) ΔH_f^o in kcal mol^{-1}; c) calculation on the ab-initio TS; d) ZPVE = zero point vibrational energy; e) activation energy according to ref. 5

the reorganization of electron distribution by the solvent. The higher dipole moment is always observed for the endo TS and at the same time these structures are favored energetically. Thus, the placement of the transition structures in a medium, even of a small dielectric constant is sufficient to revert the trend in selectivity.

The cycloaddition of acrylonitrile to cyclopentadiene was carried out in 1,4-dioxane[6,7] ($\epsilon = 2.21$), a solvent which is not considered in the GEOMOS program. We checked whether the type of solvent has any influence on the magnitude of the effect by doing calculations in n-hexane, benzene and acetonitrile in addition to those in dichloromethane. In hexane ($\epsilon = 1.98$) $\Delta E_{endo-exo} = 0.03$, in benzene ($\epsilon = 2.27$) $\Delta E_{endo-exo} = -0.18$, and in acetonitrile ($\epsilon = 35.94$) it is -0.34 kcal mol^{-1}. The trend is that any solvent defavors the exo selectivity, for the least polar one the influence is smallest and leads to almost identical ΔH^o_f values for endo and exo TS. Although acetonitrile is much more polar than dichloromethane it does not excel the influence of dichloromethane. It should be kept in mind, however, that the dielectric continuum model is only approximate and is less accurate in highly polar solvents.

Is secondary orbital overlap not important? The total energies of the TS in the "gas phase" demonstrate a preference for exo addition, i.e. secondary orbital interactions if present do not override any adverse contributions. C-2 of cyclopentadiene and the carbon atom of the nitrile group would be involved in such a stabilization. In **4** it can be seen that the possibility of a stabilizing interaction is given. However, the separation C-2,C_{CN} = 2.94 Å places some doubts on the importance of secondary overlap. Overlap decreases exponentially with distance and should be negligible at this separation. Although appealing this explanation of the often preferred endo addition doesn't seem to be very sound.



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The conclusion, therefore, is that medium effects rather than secondary orbital overlap effects are responsible for the selectivity. This seems also to be the case in other examples.[10,11]

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References

1. R. B. Woodward and R. Hoffmann, *Angew. Chem.* **1969**, *81*, 797; *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 781.
2. J. Sauer and R. Sustmann, *Angew. Chem.* **1980**, *92*, 773; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 779.
3. for a recent review see: K. N. Houk, Y. Li, and J. D. Evanseck, *Angew. Chem.* **1992**, *114*, 711.
4. M. J. S. Dewar, S. Olivella, and J. J. P. Stewart, *J. Am. Chem. Soc.* **1986**, *108*, 5771.
5. K. N. Houk, R. J. Loncharich, J. F. Blake, and W. L. Jorgensen, *J. Am. Chem. Soc.* **1989**, *111*, 9172.
6. J. Sauer, H. Wiest, and A. Mielert, *Chem. Ber.* **1964**, *97*, 3183.
7. J. Sauer, *Angew. Chem.* **1967**, *79*, 76; *Angew. Chem. Int. Ed. Engl.* **1969**, *6*, 16.
8. J. L. Pascual-Abuir, E. Silla, J. Tomasi, and R. Bonnacorsi, *J. Comput. Chem.* **1987**, *8*, 778.
9. J.-L. Rivail and D. Rinaldi, *Chem. Phys.* **1976**, *18*, 233; Program GEOMOS (QCPE 584), D. Rinaldi, P. E. Hoggan, and A. Cartier.
10. R. Sustmann, W. Sicking, H. Lamy-Schelkens, and L. Ghosez, *Tetrahedron Lett.* **1991**, *32*, 1401.
11. R. Sustmann and W. Sicking, *Tetrahedron*, submitted for publication.

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